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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/789,471	02/27/2004	Robert J. D'Amato	05213-3001 (13663.105082)	8547

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EXAMINER	
BROOKS, KRISTIE LATRICE	
ART UNIT	**PAPER NUMBER**
1616	
MAIL DATE	**DELIVERY MODE**
07/27/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/789,471	D'AMATO ET AL.	
	Examiner	Art Unit	
	Kristie Brooks	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 April 2007* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *05/16/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. Claims 1-8 are pending and are presented for examination.

2. Upon further consideration, a new ground of rejection has been entered by examiner.

3. This action is non-final.

Withdrawn Rejections/Objections

4. The Figure 3 of the drawings was objected to for not being properly labeled. The Applicant has submitted a replacement with the drawing appropriately labeled "Fig. 3" The Examiner withdraws the objection.

5. The title of the invention was not descriptive. Examiner required that it is clearly indicative of the invention to which the claims are directed. The Applicant amended the title invention to now read "Method For Inhibiting Neovascularization Using Estrogenic Compounds".

6. The abstract of the disclosure was objected to as not being descriptive enough. The Applicant amended the Abstract to set forth the compounds being utilized. The Examiner withdraws the objection.

7. The disclosure was objected to because of the following informalities: The description of Figure 3 on page 3 needs to describe panel I, II and a, b, c, and d of panel II, each individually. The Applicant amended the specification such that panels I and II and panels a, b, c, and d of panel II are described individually. The Examiner withdraws the objection.

8. The disclosure was objected to because of the following informalities: The heading for Example 4 on page 15 is included in the preceding paragraph instead of beginning on a new line. The Applicant amended the specification such that the heading for Example 4 appears as a title above the following paragraph. The Examiner withdraws the objection.

9. Claims 1-7 were rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for diseases, such as angiogenesis, characterized by abnormal cell mitosis, it does not reasonably provide enablement for neovascularization not due to angiogenesis. The Applicant has amended the claim 1 to state that the neovascularization is due to angiogenesis. Examiner is persuaded by Applicants amendments, and withdraws the rejection.

Claim Rejections - 35 USC § 112

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 1-8 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating neovascularization due to angiogenesis, does not reasonably provide enablement for inhibiting neovascularization due to angiogenesis. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims without an undue amount of experimentation.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: 1) scope or breadth of the claims; 2) nature of the invention; 3) relative level of skill possessed by one of ordinary skill in the art; 4) state of, or the amount of knowledge in, the prior art; 5) level or degree of predictability, or a lack thereof, in the art; 6) amount of guidance or direction provided by the inventor; 7) presence or absence of working examples; and 8) quantity of experimentation required to make and use the claimed invention based upon the content of the supporting disclosure. When the above factors are weighed, it is the Examiner's position that one skilled in the art could not practice the invention without undue experimentation.

1) Scope or breadth of the claims

The claims are broad. The specification merely discloses, without more, a method for treating neovascularization due to angiogenesis. However, Applicant is purporting to have a method of inhibiting neovascularization due to angiogenesis.

2) Nature of the invention

The nature of the invention is directed to a method of treating diseases characterized by abnormal cell mitosis, such as angiogenesis, and angiogenesis related diseases such as neovascularization due to angiogenesis.

3) Relative level of skill possessed by one of ordinary skill in the art

The relative level of skill possessed by one of ordinary skill in the art of medical research is relatively high, as a majority of lead investigators directing scientific research and development in this particular technological area possess an Ph.D. in a scientific discipline such as organic synthetic chemistry, polymer chemistry, medicinal chemistry, biochemistry, pharmacology, biology or the like.

4) State of, or the amount of knowledge in, the prior art

The art teaches that microtubules (MT) play a important role in eukaryotic cells. Their function and biophysical properties have made alpha-and beta-tubulin, the main components of MTs, the subject of intense study. It has been shown in the literature that tubulin is an important target molecule for developing anticancer drugs.

5) Level or degree of predictability, or a lack thereof, in the art

The art teaches that microtubules (MT) play a important role in eukaryotic cells. Their function and biophysical properties have made alpha-and beta-tubulin, the main components of MTs, the subject of intense study. It has been shown in the literature that tubulin is an important target molecule for developing anticancer drugs (see the Abstract, Islam MN et al., Microtubulin binding sites as target for developing anticancer agents, 2004, *Mini reviews in medicinal chemistry*, Dec, 4(10): Pages 1077-104). Although anticancer agents are in widespread use against both hematological malignancies and solid tumors (see the abstract, Pellegrini, et al. Review: Tubulin Function, Action of Antitubulin Drugs, and New Drug Development, 2005, C*ancer Investigation,* 23: Pages 264–273), there is still no known treatment capable of preventing conditions such as subretinal neovascualrization (see the abstract, Puig et al., 2001, Subretinal neovascularization and hemorrhages in angiod streaks, May;76 (5): Pages 309-314), thus creating a high lack of predictability as to whether the compounds of the claimed invention, will be effective at inhibiting or preventing neovascularization due to angiogenesis.

6) Amount of guidance or direction provided by the inventor

The instant specification discloses a method for treating neovascularization due to angiogenesis, but remains silent on a method of inhibiting or preventing treating neovascularization due to angiogenesis.

7) Presence or absence of working examples

The specification provides five examples showing the estrogenic compounds inhibitory effects on colchicine binding to tubulin and the inhibitory effects on tubulin polymerization in-vitro but fails to provide working embodiments of estrogenic compounds fully inhibiting or preventing of colchicine binding to tubulin and inhibitory effects on tubulin polymerization in-vitro. For example, Example 4 illustrates the percent inhibition effects on tubulin exhibited by estradiol or estradiol derivatives at a range of 30 to 82%, which fails to show any inhibition at 100%. Furthermore, the specification fails to provide working examples of how to inhibit or prevent disease associated characterized by such abnormal cell mitosis such as ocular neovascularization.

8) Quantity of experimentation required to make and use the claimed invention based upon the content of the supporting disclosure

One of ordinary skill in the art would have to conduct a tremendous number of experiments to determine which compounds are successful at inhibiting or preventing diseases characterized by abnormal cell mitosis. As a result, one of ordinary skill in the art would be required to conduct an undue amount of experimentation.

Double Patenting

12. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory

obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

13. Claims 1-8 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5 of U.S. Patent No. 6,908,910. Although the conflicting claims are not identical, they are not patentably distinct from each other because they both encompass inhibition of angiogenesis in a mammal. The instant invention differs from the cited patent by recitation of "inhibiting neovascularization" which includes inhibition of proliferation of blood vessels not encompassed by angiogenesis. Therefore, the method claimed in US Patent No. 6,908,910 is a species of the genus of the method encompassed by the instant claims, and as such it anticipates the instant invention.

14. Claims 1-8 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-14 of U.S. Patent No. 7,109,187.

Although the conflicting claims are not identical, they are not patentably distinct from each other because they both encompass inhibition of angiogenesis in a mammal. The instant invention differs from the cited patent by reciting specific mammalian diseases, i.e., treatment of specific mammalian diseases characterized by undesirable angiogenesis utilizing 2-methoxyestradiol. Therefore, the method claimed in US Patent No. 7,109,187 is a species of the genus of the method encompassed by the instant claims, and as such it anticipates the instant invention.

15. Claims 1-8 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-16 of U.S. Patent No. 7,012,070. Although the conflicting claims are not identical, they are not patentably distinct from each other because they both encompass inhibition of angiogenesis in a mammal. The instant invention differs from the cited patent by reciting specific mammalian diseases, i.e., treatment of specific mammalian diseases characterized by undesirable angiogenesis utilizing 2-methoxyestradiol. Therefore, the method claimed in US Patent No. 7,012,070 is a species of the genus of the method encompassed by the instant claims, and as such it anticipates the instant invention.

16. Claims 1-8 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1,4,6, and 8 of U.S. Patent No. 5,661,143. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are both drawn to treatment of mammalian diseases

characterized by undesirable cell mitosis. The instant invention differs from the cited patent recitation of "inhibiting neovascularization" which includes inhibition of proliferation of blood vessels not encompassed by angiogenesis. Therefore, the method claimed in US Patent No. 5,661,143 is a species of the genus of the method encompassed by the instant claims, and as such it anticipates the instant invention

17. Claims 1-8 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1,2,5, and 7 of U.S. Patent No. 5,504,074. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are both drawn o treatment of mammalian diseases characterized by undesirable angiogenesis. The instant invention differs from the cited patent recitation of "inhibiting neovascularization" which includes inhibition of proliferation of blood vessels not encompassed by angiogenesis. Therefore, the method claimed in US Patent No. 5,504,074 is a species of the genus of the method encompassed by the instant claims, and as such it anticipates the instant invention.

Note: Applicant has elected to file a terminal disclaimer when allowable subject matter is indicated in the present case. Therefore since no terminal disclaimer has been filed, this rejection is maintained.

Conclusion

18. No claims are allowed.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kristie L. Brooks whose telephone number is (571) 272-9072. The examiner can normally be reached on M-F 8:30am-6:00pm Est..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann R. Richter can be reached on (571) 272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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